REMARKS/ARGUMENTS

After entry of this paper, claims 1-4, 12, 13, 15, 28, 30, and 32-40 are pending. Claim 1 is amended to place the application in condition for allowance by deleting reference to non-naturally occurring amino acids. Applicant reserves the right to pursue this subject matter in a continuation application. Claim 15 is amended to clarify that cystine is produced within the lysosome.

Claim 38 is added to recite another embodiment and is supported in original claim 1 and on page 17, lines 24-26. Claims 37 and 39-40 recite specific cancers and are supported at page 16, lines 6-8 and page 31, lines 5-6. No new matter is added by these new claims.

Applicant notes that the amendments to the claims will not necessitate a new search to be conducted by the Examiner. Therefore, Applicant respectfully requests that any new rejections be presented in a non-final Action.

35 USC § 112, Second Paragraph Rejection

> *Claim 15 is rejected under this section for assertedly being indefinite. The Examiner asserted that the phrase "upon exposure to a susceptible cell increases the cell's intralysosomal cystine level above 0.5 nmol/mg cell protein" and indicated that it is unclear if the cystine level increases in the lysosome or the cystine concentration in lysosomal protein increases.*

Applicant respectfully requests reconsideration and withdrawal of this rejection for the following reasons.

One of skill in the art would understand that cystine is produced in and/or may be transported into a cell's lysosome not in the lysosomal protein. To support this knowledge in the art at the time of the priority date, Applicant provides the following documents. For the Examiner's information, these documents are included in an Information Disclosure Statement submitted herewith.

- Smith et al., "*Lysosomal Cystine Transport*", J. Biol. Chem., 262(3):1244-1253 (January 25, 1987)
- Oshima et al., "*Cystine Metabolism in Human Fibroblasts*", J. Biol. Chem., 251(14):3287-3293 (July 25, 1976)

- Cherqui et al., "*Intralysosomal Cystine Accumulation in Mice Lacking Cystinosin, the Protein Defective in Cystinosis*", Mol. Cell. Biol., 22(21):7622-7632 (November, 2002)

As the Examiner will note, all of these documents make it scientifically clear that cystine is produced and/or may be transported into a cell's lysosome. See, *e.g.*, page 4292, column 1, paragraphs 3 and 4 and Figure 5 of Oshima; the entire Smith document; and page 7622, column 1, paragraph 1 of Cherqui.

Withdrawal of this rejection is requested.

35 USC § 112, First Paragraph Rejection

Claims 1, 4, 12, 15, 28, 32, 35, and 36 are rejected under this section for assertedly lacking written description.

The Examiner asserted that the specification does not adequately support the use of compounds other than CDME. The Examiner indicated that the instant specification supports the study of CDME in breast tumor cell lines and in vivo studies in nude mice

Applicant respectfully requests reconsideration and withdrawal of this rejection for the following reasons.

The Examiner asserted that "[e]ven with only 20 natural amino acids if m=20, the number of compounds that the formula as depicted above represents 20^{20} molecules..."[1] and "[f]urther inclusion of any and all known and unknown non-natural amino acids and inclusion of 'R1" variable as a substituted or unsubstituted alkyl of 1-10 carbon atoms, introduces even more complexity to the molecule".[2] With respect, the mere fact that 20 natural amino acids would result in a number of feasible compounds is not the standard by which a determination of compliance with the written description requirement should be made. Nor is the fact that the R1 variable may "introduce complexity" the standard by which the claims should be evaluated to determine if they comply with the written description requirement.

Instead, and as the Examiner is aware, the level of skill in the art is a major factor which must be considered in determining if the specification supports one or

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1 Page 7, lines 1-3 of the Office Action dated July 9, 2008

2 Page 7, lines 4-6 of the Office Action dated July 9, 2008

more claims of an application. Clearly, page 4, line 22 through page 5, line 1 of the specification provides a very detailed description of the length of an "alkyl" group and the possible substituents that may be attached to one or more carbon atoms of the alkyl group. Further, although unnecessary, Applicant also provided the list of 20 natural amino acids on page 5, lines 5-12 of the specification. Given the knowledge in the art at the priority date and the teachings of this specification, one of skill in the art would be able to physically prepare different compounds by performing the following substitutions, if so desired, in the claimed compound:

- different alkyl groups of R_1, *i.e.*, an ethyl group instead of a methyl group
- different substitutions of an alkyl group of R_1, *i.e.*, a methyl group substituted by a halogen for a methyl group substituted by a cyano group
- one amino acid for another in "X", *i.e.*, a glycine for a glutamine.

The ability in the art to prepare such compounds and use routine techniques to utilize the same in a pharmaceutical composition, specifically for treating cancer, is within what can be expected for one practicing the claimed invention. The assertion that the specification provides data for only one (1) example of a compound, i.e., CDME, should not be patentability-destroying as applied to written description. Instead, the Examiner is required to turn to the teachings of the application and knowledge in the art.

Further, while the specification provides one (1) example of treating breast cancer, Applicant provides other cancers on page 16, lines 6-14 which may be treated using the pharmaceutical composition as claimed in the present application. One of skill in the art would be able to perform assays as described in the specification to determine if the compounds induce apoptosis in a variety of cancer cells. The procedures as set forth in specification and specifically the examples can be readily followed by one of skill in the art to determine if the claimed compounds were useful in treating the claimed cancer. Similarly, conventional experimental animal models of various cancers may be readily used to assess the utility of these compounds in treatments of cancers other than breast cancer. No undue experimentation would be necessary by one of skill in the art.

Withdrawal of this rejection is requested.

35 USC § 102(b) Rejections

(i) Claims 1, 4, 12, 15, 33, and 36 are rejected as allegedly anticipated by Kitazawa (2002, FEBS Letters, 526:106-100).

The Examiner asserted that Kitazawa discusses the N-acetyl salt of CDME in cell culture medium and therefore teaches the rejected claims. The Examiner also indicated that the phrase "for the treatment of cancer" is an intended use and does not provide limitations as to any structural element necessary in the compound or composition.

Applicant respectfully requests reconsideration and withdrawal of this rejection for the following reasons.

Kitazawa discusses the use of N,N'-diacetyl-L-cystine dimethyl ester (DACDM) on the UVB-induced NK-κB binding activity in a human keratinocyte cell line. Kitazawa specifically discusses growing the HaCaT cell line in DMEM supplemented with 10% FBS, seeding these cells into 96-well microplates, and culturing with DACDM. Kitazawa does not discuss a composition containing DACDM and a **pharmaceutically acceptable carrier**. Clearly, the culture medium of Kitazawa, *i.e.*, DMEM/FBS, is not a pharmaceutically acceptable carrier. Nor would one of skill in the art believe that it could be used as such. Therefore, Kitazawa does not teach the pending claims.

Withdrawal of this rejection is requested.

(ii) Claims 1, 4, 15, 28, 30, 33, and 34 are rejected as allegedly anticipated by Pisoni (1992, Somatic Cell and Molecular Genetics, 18:1-6).

The Examiner asserted that Pisoni discusses CDME in culture medium which meets the limitation for the claimed composition. The Examiner also indicated that the phrase "for the treatment of cancer" is an intended use and does not provide limitations as to any structural element necessary in the compound or composition.

Applicant respectfully requests reconsideration and withdrawal of this rejection for the following reasons.

Pisoni discusses measuring cystine content of cystinotic fibroblasts after incubation with CDME. Pisoni specifically discusses combining the human

fibroblasts with CDME in culture medium including 10% fetal calf serum, which was then washed using phosphate buffered saline (PBS) and trypsin. Pisoni does not discuss a composition containing CDME and a **pharmaceutically acceptable carrier**. Clearly, the culture medium of Pisoni, *i.e.*, fetal calf serum, is not a pharmaceutically acceptable carrier. Nor would one of skill in the art believe that it could be used as such.

Further, Pisoni does not discuss the treatment of any disorders, particularly cancer. Instead, Pisoni is directed toward understanding cystinosis, which is a rare inherited disease caused by a human mutation, and specifically affecting intralysosomal cystine transport. It is unrelated to cancer. Therefore, Pisoni does not teach the pending claims.

Withdrawal of this rejection is requested.

The Director is hereby authorized to charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account No. 08-3040.

Respectfully submitted,

HOWSON & HOWSON LLP
Attorney for Applicant

Mary E. Bak

Mary E. Bak
Registration No. 31,215
501 Office Center Drive
Suite 210
Fort Washington, PA 19034
Telephone: 215-540-9200
Facsimile: 215-540-5818